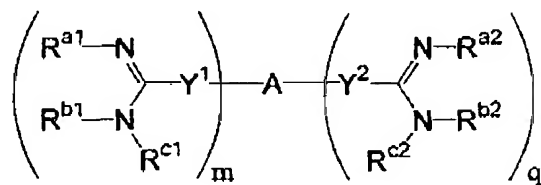


Application No. 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

Docket No.: NBI-105CN

Listing of Claims:

1. **(original)** A method of treating or preventing an amyloid-related disease in a subject comprising administering to said subject a therapeutic amount of an amidine compound.
2. **(cancelled)**.
3. **(original)** The method according to claim 1, wherein said compound is a bis(amidine) compound.
4. **(original)** The method according to claim 1, wherein said compound is a bis(benzamidine) compound.
5. **(currently amended)** The method according to claim 1, wherein said compound is selected according to the following Formula, ~~such that amyloid fibril formation or deposition, neurodegeneration, or cellular toxicity is reduced or inhibited:~~



(Formula X)

wherein each R^{a1} , R^{b1} , R^{c1} , R^{a2} , R^{b2} , and R^{c2} is independently a hydrogen, a Z group, or R^{a1} and R^{b1} or R^{a2} and R^{b2} are both taken together along with the nitrogen atoms to which they are bound to form a ring structure;

each of Y^1 and Y^2 is independently a direct bond or a linking moiety;

m and q are each independently an integer selected from zero to five inclusive, such that $2 \leq m+q \leq 5$; and

A is a carrier moiety selected from substituted or unsubstituted aliphatic and aromatic groups, and combinations thereof; such that the Y^1 and Y^2 moieties are bonded to an aromatic group;

Application No.: 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

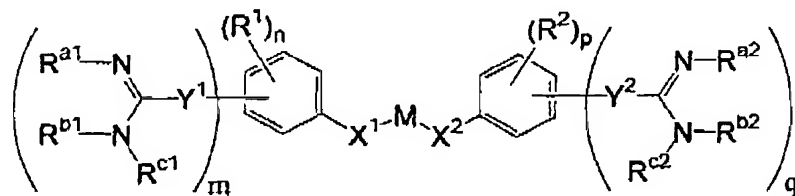
Docket No.: NBI-105CN

Z is a substituted or unsubstituted moiety selected from straight or branched alkyl, cycloalkyl, alkoxy, thioalkyl, alkenyl, alkynyl, heterocyclic, carbocyclic, aryl, aryloxy, aralkyl, aryloxyalkyl, arylacetamidoyl, alkylaryl, heteroaralkyl, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, or heteroaryl group, $(CR'R'')_{0-10}NR'R''$, $(CR'R'')_{0-10}CN$, NO_2 , halogen, $(CR'R'')_{0-10}C(halogen)_3$, $(CR'R'')_{0-10}CH(halogen)_2$, $(CR'R'')_{0-10}CH_2(halogen)$, $(CR'R'')_{0-10}CONR'R''$, $(CR'R'')_{0-10}(CNH)NR'R''$, $(CR'R'')_{0-10}S(O)_{1-2}NR'R''$, $(CR'R'')_{0-10}CHO$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(O)_{0-3}R'$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(CR'R'')_{0-3}H$, $(CR'R'')_{0-10}OH$, $(CR'R'')_{0-10}COR'$, $(CR'R'')_{0-10}$ (substituted or unsubstituted phenyl), $(CR'R'')_{0-10}(C_3-C_8 \text{ cycloalkyl})$, $(CR'R'')_{0-10}CO_2R'$, or $(CR'R'')_{0-10}OR'$ group, or the side chain of any naturally occurring amino acid;

R' and R'' are each independently hydrogen, a C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, or aryl group, or R' and R'' taken together are a benzylidene group or a $-(CH_2)_2O(CH_2)_2-$ group;

and pharmaceutically acceptable salts thereof.

6. **(currently amended)** The method according to claim 1, wherein said compound is selected according to the following Formula, ~~such that amyloid fibril formation or deposition, neurodegeneration, or cellular toxicity is reduced or inhibited:~~



(Formula 1)

wherein each R^{a1} , R^{b1} , R^{c1} , R^{a2} , R^{b2} , and R^{c2} is independently a hydrogen, a Z group, or R^{a1} and R^{b1} or R^{a2} and R^{b2} are both taken together along with the nitrogen atoms to which they are bound to form a ring structure;

each of Y^1 and Y^2 is independently a direct bond or a linking moiety;

each of R^1 and R^2 is independently a hydrogen or a Z group, or two adjacent or proximate R^1

Application No.: 10/731,463
Preliminary Amendment
Filed February 09, 2004

Docket No.: NBI-105CN

or R² groups taken together with the ring to which they are bound form a fused aromatic, heteroaromatic, cycloalkyl, or heterocyclic structure;

each of X¹ and X² is independently an alkylene group, an oxygen, a NR' group (where R' is hydrogen, a C₁-C₅ alkyl, C₂-C₅ alkenyl, C₂-C₅ alkynyl, or aryl group), a sulfonamide group, a carbonyl, amide, C₁-C₅ alkylene group, C₂-C₅ alkenyl group, C₂-C₅ alkynyl group, or a sulfur atom, or combinations thereof or a direct bond;

M is an alkylene group, an alkenylene group, an alkynylene group, an alkoxyalkylene group, an alkylaminoalkylene group, a thioalkoxyalkylene group, an arylenedialkylene group, an alkylenediarylene group, a heteroarylenedialkylene group, an arylene group, a heteroarylene group, an oligoetheral or oligo(alkyleneoxide) group, or an arylene-di(oligoalkyleneoxide) group, each of which may be substituted or unsubstituted;

Z is a substituted or unsubstituted moiety selected from straight or branched alkyl, cycloalkyl, alkoxy, thioalkyl, alkenyl, alkynyl, heterocyclic, carbocyclic, aryl, aryloxy, aralkyl, aryloxyalkyl, arylacetamidoyl, alkylaryl, heteroaralkyl, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, or heteroaryl group, (CR'R'')₀₋₁₀NR'R'', (CR'R'')₀₋₁₀CN, NO₂, halogen, (CR'R'')₀₋₁₀C(halogen)₃, (CR'R'')₀₋₁₀CH(halogen)₂, (CR'R'')₀₋₁₀CH₂(halogen), (CR'R'')₀₋₁₀CONR'R'', (CR'R'')₀₋₁₀(CNH)NR'R'', (CR'R'')₀₋₁₀S(O)₁₋₂NR'R'', (CR'R'')₀₋₁₀CHO, (CR'R'')₀₋₁₀O(CR'R'')₀₋₁₀H, (CR'R'')₀₋₁₀S(O)₀₋₃R', (CR'R'')₀₋₁₀O(CR'R'')₀₋₁₀H, (CR'R'')₀₋₁₀S(CR'R'')₀₋₃H, (CR'R'')₀₋₁₀OH, (CR'R'')₀₋₁₀COR', (CR'R'')₀₋₁₀(substituted or unsubstituted phenyl), (CR'R'')₀₋₁₀(C₃-C₈ cycloalkyl), (CR'R'')₀₋₁₀CO₂R', or (CR'R'')₀₋₁₀OR' group, or the side chain of any naturally occurring amino acid;

R' and R'' are each independently hydrogen, a C₁-C₅ alkyl, C₂-C₅ alkenyl, C₂-C₅ alkynyl, or aryl group, or R' and R'' taken together are a benzylidene group or a -(CH₂)₂O(CH₂)₂- group;

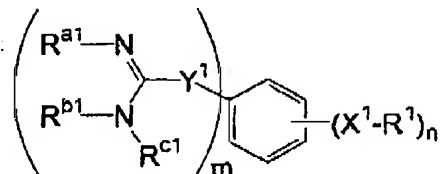
m and q are each independently an integer selected from zero to four inclusive, and n and p are each independently an integer selected from zero to four inclusive, such that m+n=5 and p+q=5, wherein either m or q is at least one;

and pharmaceutically acceptable salts thereof.

Application No.: 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

Docket No.: NBI-105CN

7. (currently amended) The method according to claim 1, wherein said compound is selected according to the following Formula, ~~such that amyloid fibril formation or deposition, neurodegeneration, or cellular toxicity is reduced or inhibited:~~



(Formula II)

wherein each R^{a1} , R^{b1} , R^{c1} , R^{a2} , R^{b2} , and R^{c2} is independently a hydrogen, a Z group other than a substituted aryl group or a substituted alkyl group, or R^{a1} and R^{b1} or R^{a2} and R^{b2} are both taken together along with the nitrogen atoms to which they are bound to form a ring structure;

Y^1 is a direct bond or a linking moiety;

R^1 is a hydrogen or a Z group, or two adjacent or proximate R^1 groups taken together with the corresponding X^1 groups and the ring to which they are bound form a fused aromatic, heteroaromatic, cycloalkyl, or heterocyclic structure;

X^1 is an alkylene group, an oxygen, a NR' group (where R' is hydrogen, a C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, or aryl group), a sulfonamide group, a carbonyl, amide, C_1 - C_5 alkylene group, C_2 - C_5 alkenyl group, C_2 - C_5 alkynyl group, or a sulfur atom, or combinations thereof or a direct bond;

Z is a substituted or unsubstituted moiety selected from straight or branched alkyl, cycloalkyl, alkoxy, thioalkyl, alkenyl, alkynyl, heterocyclic, carbocyclic, aryl, aryloxy, aralkyl, aryloxyalkyl, arylacetamidoyl, alkylaryl, heteroaralkyl, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, or heteroaryl group, $(CR'R'')_{0-10}NR'R''$, $(CR'R'')_{0-10}CN$, NO_2 , halogen, $(CR'R'')_{0-10}C(halogen)_3$, $(CR'R'')_{0-10}CH(halogen)_2$, $(CR'R'')_{0-10}CH_2(halogen)$, $(CR'R'')_{0-10}CONR'R''$, $(CR'R'')_{0-10}(CNH)NR'R''$, $(CR'R'')_{0-10}S(O)_{1-2}NR'R''$, $(CR'R'')_{0-10}CHO$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(O)_{0-3}R'$.

Application No.: 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

Docket No.: NBI-105CN

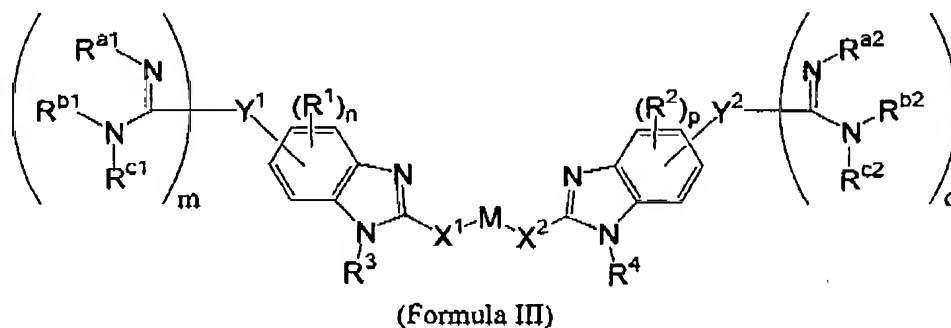
$(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(CR'R'')_{0-3}H$, $(CR'R'')_{0-10}OH$, $(CR'R'')_{0-10}COR'$, $(CR'R'')_{0-10}$ (substituted or unsubstituted phenyl), $(CR'R'')_{0-10}(C_3-C_8$ cycloalkyl), $(CR'R'')_{0-10}CO_2R'$, or $(CR'R'')_{0-10}OR'$ group, or the side chain of any naturally occurring amino acid;

R' and R'' are each independently hydrogen, a C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, or aryl group, or R' and R'' taken together are a benzylidene group or a $-(CH_2)_2O(CH_2)_2-$ group;

m is an integer selected from one to six inclusive, and n is an integer selected from zero to five inclusive, such that $m+n=6$;

and pharmaceutically acceptable salts thereof.

8. **(currently amended)** The method according to claim 1, wherein said therapeutic compound is selected according to the following Formula, ~~such that amyloid fibril formation or deposition, neurodegeneration, or cellular toxicity is reduced or inhibited:~~



wherein each R^{a1} , R^{b1} , R^{c1} , R^{a2} , R^{b2} , and R^{c2} is independently a hydrogen, a Z group, or R^{a1} and R^{b1} or R^{a2} and R^{b2} are both taken together along with the nitrogen atoms to which they are bound to form a ring structure;

each of Y^1 and Y^2 is independently a direct bond or a linking moiety;

each of R^1 and R^2 is independently a hydrogen or a Z group, or two adjacent or proximate R^1 or R^2 groups taken together with the ring to which they are bound form a fused aromatic, heteroaromatic, cycloalkyl, or heterocyclic structure;

Application No.: 10/731,463
Preliminary Amendment
Filed February 09, 2004

Docket No.: NBI-105CN

each of R^3 and R^4 is independently selected from the group consisting of hydrogen, substituted or unsubstituted straight or branched alkyl, cycloalkyl, carbocyclic, aryl, heterocyclic, and heteroaryl;

each of X^1 and X^2 is independently an alkylene group, an oxygen, a NR' group (where R' is hydrogen, a C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, or aryl group), a sulfonamide group, a carbonyl, amide, C_1 - C_5 alkylene group, C_2 - C_5 alkenyl group, C_2 - C_5 alkynyl group, or a sulfur atom, or combinations thereof or a direct bond;

M is an alkylene group, an alkenylene group, an alkynylene group, an alkoxyalkylene group, an alkylaminoalkylene group, a thioalkoxyalkylene group, an arylenedialkylene group, an alkylenediarylene group, a heteroarylenedialkylene group, an arylene group, a heteroarylene group, an oligoetheral or oligo(alkyleneoxide) group, or an arylene-di(oligoalkyleneoxide) group, each of which may be substituted or unsubstituted;

Z is a substituted or unsubstituted moiety selected from straight or branched alkyl, cycloalkyl, alkoxy, thioalkyl, alkenyl, alkynyl, heterocyclic, carbocyclic, aryl, aryloxy, aralkyl, aryloxyalkyl, arylacetamidoyl, alkylaryl, heteroaralkyl, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, or heteroaryl group, $(CR'R'')_{0-10}NR'R''$, $(CR'R'')_{0-10}CN$, NO_2 , halogen, $(CR'R'')_{0-10}C(halogen)_3$, $(CR'R'')_{0-10}CH(halogen)_2$, $(CR'R'')_{0-10}CH_2(halogen)$, $(CR'R'')_{0-10}CONR'R''$, $(CR'R'')_{0-10}(CNH)NR'R''$, $(CR'R'')_{0-10}S(O)_{1-2}NR'R''$, $(CR'R'')_{0-10}CHO$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(O)_{0-3}R'$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(CR'R'')_{0-3}H$, $(CR'R'')_{0-10}OH$, $(CR'R'')_{0-10}COR'$, $(CR'R'')_{0-10}(\text{substituted or unsubstituted phenyl})$, $(CR'R'')_{0-10}(C_3-C_8 \text{ cycloalkyl})$, $(CR'R'')_{0-10}CO_2R'$, or $(CR'R'')_{0-10}OR'$ group, or the side chain of any naturally occurring amino acid;

R' and R'' are each independently hydrogen, a C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, or aryl group, or R' and R'' taken together are a benzyldiene group or a $-(CH_2)_2O(CH_2)_2-$ group;

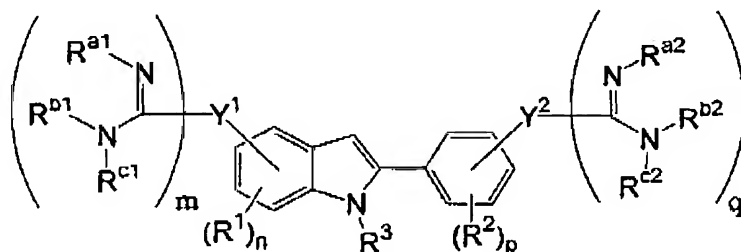
m, n, p, and q are each independently an integer selected from zero to three inclusive, $m+n \leq 4$, $p+q \leq 4$, and $m+q \geq 1$;

and pharmaceutically acceptable salts thereof.

Application No.: 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

Docket No.: NBI-105CN

9. (currently amended) The method according to claim 1, wherein said compound is selected according to the following Formula, ~~such that amyloid fibril formation or deposition, neurodegeneration, or cellular toxicity is reduced or inhibited:~~



(Formula IV)

wherein each R^{a1} , R^{b1} , R^{c1} , R^{a2} , R^{b2} , and R^{c2} is independently a hydrogen, a Z group, or R^{a1} and R^{b1} or R^{a2} and R^{b2} are both taken together along with the nitrogen atoms to which they are bound to form a ring structure;

each of Y^1 and Y^2 is independently a direct bond or a linking moiety;

each of R^1 and R^2 is independently a hydrogen or a Z group, or two adjacent or proximate R^1 or R^2 groups taken together with the ring to which they are bound form a fused aromatic, heteroaromatic, cycloalkyl, or heterocyclic structure;

R^3 is selected from the group consisting of hydrogen, substituted or unsubstituted straight or branched alkyl, cycloalkyl, carbocyclic, aryl, heterocyclic, and heteroaryl;

Z is a substituted or unsubstituted moiety selected from straight or branched alkyl, cycloalkyl, alkoxy, thioalkyl, alkenyl, alkynyl, heterocyclic, carbocyclic, aryl, aryloxy, aralkyl, aryloxyalkyl, arylacetamidoyl, alkylaryl, heteroaralkyl, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, or heteroaryl group, $(CR'R'')_{0-10}NR'R''$, $(CR'R'')_{0-10}CN$, NO_2 , halogen, $(CR'R'')_{0-10}C(halogen)_3$, $(CR'R'')_{0-10}CH(halogen)_2$, $(CR'R'')_{0-10}CH_2(halogen)$, $(CR'R'')_{0-10}CONR'R''$, $(CR'R'')_{0-10}(CNH)NR'R''$, $(CR'R'')_{0-10}S(O)_{1-2}NR'R''$, $(CR'R'')_{0-10}CHO$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(O)_{0-3}R'$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(CR'R'')_{0-3}H$, $(CR'R'')_{0-10}OH$, $(CR'R'')_{0-10}COR'$, $(CR'R'')_{0-10}(substituted\ or\ unsubstituted\ phenyl)$, $(CR'R'')_{0-10}(C_3-C_8\ cycloalkyl)$,

Application No.: 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

Docket No.: NBI-105CN

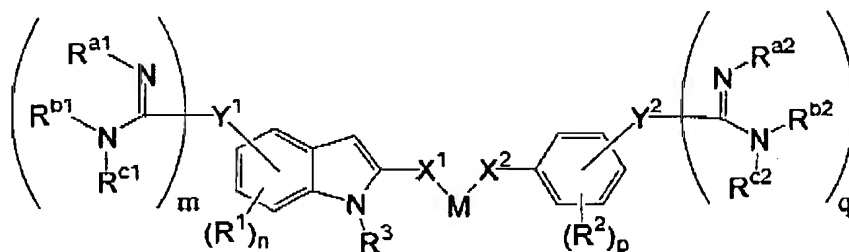
$(CR'R'')_{0-10}CO_2R'$, or $(CR'R'')_{0-10}OR'$ group, or the side chain of any naturally occurring amino acid;

R' and R'' are each independently hydrogen, a C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, or aryl group, or R' and R'' taken together are a benzylidene group or a $-(CH_2)_2O(CH_2)_2-$ group;

m and n are each independently an integer selected from zero to three inclusive, p and q are each independently an integer selected from zero to four inclusive, $m+n \leq 4$, $p+q \leq 5$, and $m+q \geq 1$;

and pharmaceutically acceptable salts thereof.

10. **(currently amended)** The method according to claim 1, wherein said compound is selected according to the following Formula, ~~such that amyloid fibril formation or deposition, neurodegeneration, or cellular toxicity is reduced or inhibited:~~



(Formula IVb)

wherein each R^{a1} , R^{b1} , R^{c1} , R^{a2} , R^{b2} , and R^{c2} is independently a hydrogen, a Z group, or R^{a1} and R^{b1} or R^{a2} and R^{b2} are both taken together along with the nitrogen atoms to which they are bound to form a ring structure;

each of Y^1 and Y^2 is independently a direct bond or a linking moiety;

each of R^1 and R^2 is independently a hydrogen or a Z group, or two adjacent or proximate R^1 or R^2 groups taken together with the ring to which they are bound form a fused aromatic, heteroaromatic, cycloalkyl, or heterocyclic structure;

R^3 is selected from the group consisting of hydrogen, substituted or unsubstituted straight or

Application No.: 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

Docket No.: NBI-105CN

branched alkyl, cycloalkyl, carbocyclic, aryl, heterocyclic, and heteroaryl;

each of X^1 and X^2 is independently an alkylene group, an oxygen, a NR' group (where R' is hydrogen, a C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, or aryl group), a sulfonamide group, a carbonyl, amide, C_1 - C_5 alkylene group, C_2 - C_5 alkenyl group, C_2 - C_5 alkynyl group, or a sulfur atom, or combinations thereof or a direct bond;

M is an alkylene group, an alkenylene group, an alkynylene group, an alkoxyalkylene group, an alkylaminoalkylene group, a thioalkoxyalkylene group, an arylenedialkylene group, an alkylenediarylene group, a heteroarylenedialkylene group, an arylene group, a heteroarylene group, an oligoetheral or oligo(alkyleneoxide) group, or an arylene-di(oligoalkyleneoxide) group, each of which may be substituted or unsubstituted;

Z is a substituted or unsubstituted moiety selected from straight or branched alkyl, cycloalkyl, alkoxy, thioalkyl, alkenyl, alkynyl, heterocyclic, carbocyclic, aryl, aryloxy, aralkyl, aryloxyalkyl, arylacetamidoyl, alkylaryl, heteroaralkyl, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, or heteroaryl group, $(CR'R'')_{0-10}NR'R''$, $(CR'R'')_{0-10}CN$, NO_2 , halogen, $(CR'R'')_{0-10}C(halogen)_3$, $(CR'R'')_{0-10}CH(halogen)_2$, $(CR'R'')_{0-10}CH_2(halogen)$, $(CR'R'')_{0-10}CONR'R''$, $(CR'R'')_{0-10}(CNH)NR'R''$, $(CR'R'')_{0-10}S(O)_{1-2}NR'R''$, $(CR'R'')_{0-10}CHO$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(O)_{0-3}R'$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(CR'R'')_{0-3}H$, $(CR'R'')_{0-10}OH$, $(CR'R'')_{0-10}COR'$, $(CR'R'')_{0-10}(\text{substituted or unsubstituted phenyl})$, $(CR'R'')_{0-10}(C_3-C_8 \text{ cycloalkyl})$, $(CR'R'')_{0-10}CO_2R'$, or $(CR'R'')_{0-10}OR'$ group, or the side chain of any naturally occurring amino acid;

R' and R'' are each independently hydrogen, a C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, or aryl group, or R' and R'' taken together are a benzylidene group or a $-(CH_2)_2O(CH_2)_2-$ group;

m and n are each independently an integer selected from zero to three inclusive, p and q are each independently an integer selected from zero to four inclusive, $m+n \leq 4$, $p+q \leq 5$, and $m+q \geq 1$;

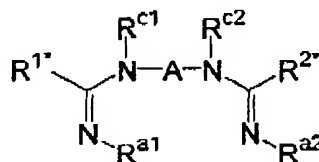
and pharmaceutically acceptable salts thereof.

11. **(currently amended)** The method according to claim 1, wherein said compound is selected according to the following Formula, ~~such that amyloid fibril formation or deposition;~~

Application No.. 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

Docket No.: NBI-105CN

~~neurodegeneration, or cellular toxicity is reduced or inhibited:~~



(Formula V)

wherein each R^{a1} , R^{b1} , R^{c1} , R^{a2} , R^{b2} , and R^{c2} is independently a hydrogen, a Z group, or R^{a1} and R^{b1} or R^{a2} and R^{b2} are both taken together along with the nitrogen atoms to which they are bound to form a ring structure;

A is a carrier moiety selected from substituted or unsubstituted aliphatic and aromatic groups, and combinations thereof; such that the Y^1 and Y^2 moieties are bonded to an aromatic group;

Z is a substituted or unsubstituted moiety selected from straight or branched alkyl, cycloalkyl, alkoxy, thioalkyl, alkenyl, alkynyl, heterocyclic, carbocyclic, aryl, aryloxy, aralkyl, aryloxyalkyl, arylacetamidoyl, alkylaryl, heteroaralkyl, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, or heteroaryl group, $(CR'R'')_{0-10}NR'R''$, $(CR'R'')_{0-10}CN$, NO_2 , halogen, $(CR'R'')_{0-10}C(halogen)_3$, $(CR'R'')_{0-10}CH(halogen)_2$, $(CR'R'')_{0-10}CH_2(halogen)$, $(CR'R'')_{0-10}CONR'R''$, $(CR'R'')_{0-10}(CNH)NR'R''$, $(CR'R'')_{0-10}S(O)_{1-2}NR'R''$, $(CR'R'')_{0-10}CHO$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(O)_{0-3}R'$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(CR'R'')_{0-3}H$, $(CR'R'')_{0-10}OH$, $(CR'R'')_{0-10}COR'$, $(CR'R'')_{0-10}(\text{substituted or unsubstituted phenyl})$, $(CR'R'')_{0-10}(C_3-C_8 \text{ cycloalkyl})$, $(CR'R'')_{0-10}CO_2R'$, or $(CR'R'')_{0-10}OR'$ group, or the side chain of any naturally occurring amino acid;

R' and R'' are each independently hydrogen, a C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, or aryl group, or R' and R'' taken together are a benzylidene group or a $-(CH_2)_2O(CH_2)_2-$ group;

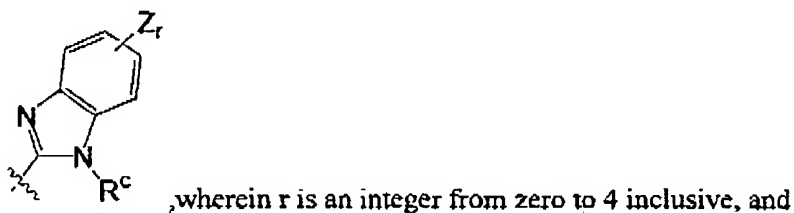
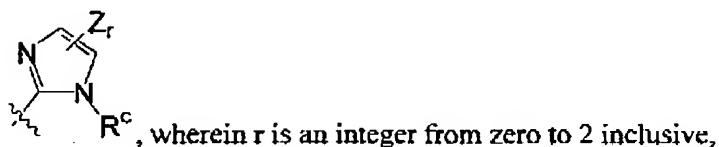
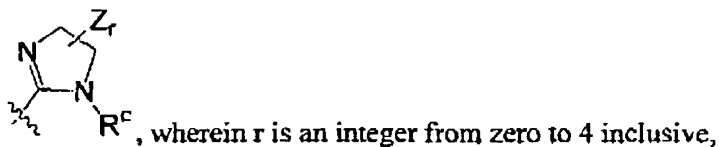
and pharmaceutically acceptable salts thereof.

12. **(currently amended)** The method according to claim 1, wherein said amyloid-related disease is ~~an A β amyloid related disease~~ associated with amyloid- β .

Application No.. 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

Docket No.: NBI-105CN

13. (original) The method according to claim 1, wherein said amyloid-related disease is Alzheimer's disease, cerebral amyloid angiopathy, Down's syndrome, or inclusion body myositis.
14. (original) The method according to claim 1, wherein said amyloid-related disease is type II diabetes.
15. (original) The method according to claim 1, where said subject is a human.
16. (currently amended) The method according to claim 5, wherein said ring structure is selected from the following:



Z and R^c are as defined in claim 5 are each independently a substituted or unsubstituted moiety selected from straight or branched alkyl, cycloalkyl, alkoxy, thioalkyl, alkenyl, alkynyl, heterocyclic, carbocyclic, aryl, aryloxy, aralkyl, aryloxyalkyl, arylacetamidovl, alkylaryl, heteroaralkyl, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, or heteroaryl

Application No.: 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

Docket No.: NBI-105CN

group, (CR'R'')₀₋₁₀NR'R'', (CR'R'')₀₋₁₀CN, NO₂, halogen, (CR'R'')₀₋₁₀C(halogen)₃, (CR'R'')₀₋₁₀CH(halogen)₂, (CR'R'')₀₋₁₀CH₂(halogen), (CR'R'')₀₋₁₀CONR'R'', (CR'R'')₀₋₁₀(CNH)NR'R'', (CR'R'')₀₋₁₀S(O)₁₋₂NR'R'', (CR'R'')₀₋₁₀CHO, (CR'R'')₀₋₁₀O(CR'R'')₀₋₁₀H, (CR'R'')₀₋₁₀S(O)₀₋₃R', (CR'R'')₀₋₁₀O(CR'R'')₀₋₁₀H, (CR'R'')₀₋₁₀S(CR'R'')₀₋₃H, (CR'R'')₀₋₁₀OH, (CR'R'')₀₋₁₀COR', (CR'R'')₀₋₁₀(substituted or unsubstituted phenyl), (CR'R'')₀₋₁₀(C₃-C₈ cycloalkyl), (CR'R'')₀₋₁₀CO₂R', or (CR'R'')₀₋₁₀OR' group, or the side chain of any naturally occurring amino acid; and

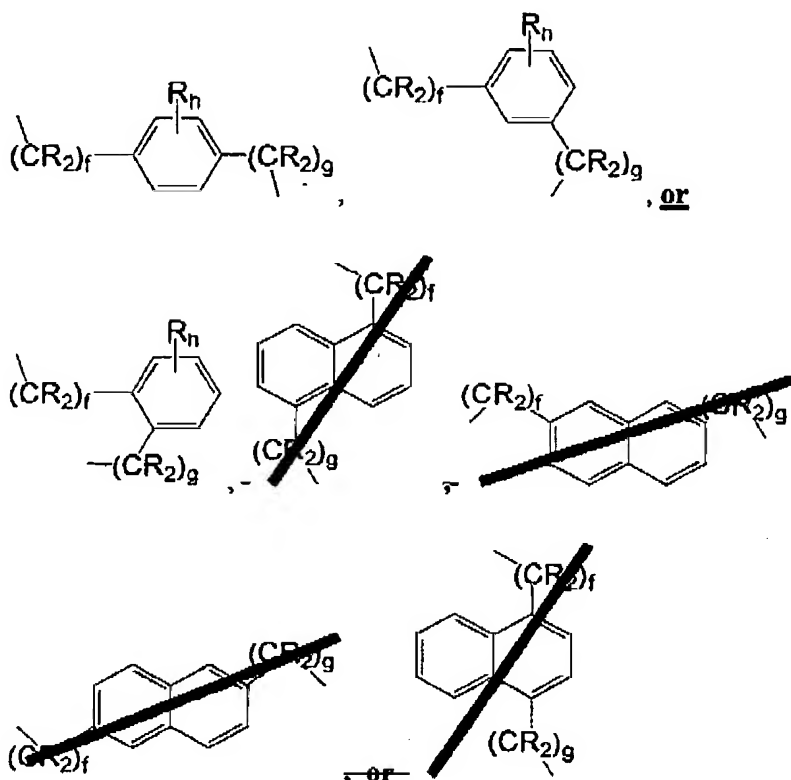
R' and R'' are each independently hydrogen, a C₁-C₆ alkyl, C₂-C₅ alkenyl, C₂-C₅ alkynyl, or aryl group, or R' and R'' taken together are a benzylidene group or a -(CH₂)₂O(CH₂)₂- group.

17. (original) The method according to claim 5, wherein each of said R^{a1}, R^{b1}, R^{c1}, R^{a2}, R^{b2}, and R^{c2} groups is a hydrogen, hydroxy group, a substituted or unsubstituted C₁-C₈ alkyl or C₁-C₈ alkoxy group.
18. (original) The method according to claim 5, wherein each of said R^{a1}, R^{b1}, R^{c1}, R^{a2}, R^{b2}, and R^{c2} groups is an aromatic group or heteroaromatic group.
19. (currently amended) The method according to claim 5, wherein each of said R^{a1}, R^{b1}, R^{c1}, R^{a2}, R^{b2}, and R^{c2} groups is a ~~R³ group as defined in claim 9~~ hydrogen, substituted or unsubstituted straight or branched alkyl, cycloalkyl, carbocyclic, aryl, heterocyclic, or heteroaryl group.
20. (original) The method according to claim 5, wherein each of said Y¹ and Y² groups is a linking moiety of less than about 75 molecular weight.
21. (original) The method according to claim 5, wherein said Y¹ and Y² groups is a direct bond.
22. (original) The method according to claim 6, wherein each of said R¹ and R² groups is independently a hydrogen, a substituted or unsubstituted C₁-C₈ alkyl group, a substituted or unsubstituted C₁-C₈ alkenyl group, a halogen, a substituted or unsubstituted aryl or heteroaryl group, a substituted or unsubstituted amino group, a nitro group, or a substituted or unsubstituted C₁-C₈ alkoxy group.
23. (original) The method according to claim 6, wherein said M group is -[(CH₂)₅O]_t(CH₂)_s-, where t is 1 to 6 and s is 2 to 6.

Application No.: 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

Docket No.: NBI-105CN

24. **(original)** The method according to claim 6, wherein said M group is a phenylenedialkylene group.
25. **(currently amended)** The method according to claim 6, wherein said M arylene dialkylene group is



wherein each R group is independently a hydrogen or is ~~selected from the group Z as defined in claim 5,~~ a substituted or unsubstituted moiety selected from straight or branched alkyl, cycloalkyl, alkoxy, thioalkyl, alkenyl, alkynyl, heterocyclic, carbocyclic, aryl, aryloxy, aralkyl, aryloxyalkyl, arylacetamidovyl, alkylaryl, heteroaralkyl, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, or heteroaryl group. $(CR'R'')_{0-10}NR'R''$, $(CR'R'')_{0-10}CN$, NO_2 , halogen, $(CR'R'')_{0-10}C(halogen)_3$, $(CR'R'')_{0-10}CH(halogen)_2$, $(CR'R'')_{0-10}CH_2(halogen)$, $(CR'R'')_{0-10}CONR'R''$, $(CR'R'')_{0-10}(CNH)NR'R''$, $(CR'R'')_{0-10}S(O)_{1-2}NR'R''$, $(CR'R'')_{0-10}CHO$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(O)_{0-3}R'$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(CR'R'')_{0-3}H$, $(CR'R'')_{0-10}OH$, $(CR'R'')_{0-10}COR'$, $(CR'R'')_{0-10}$ (substituted or unsubstituted phenyl).

Application No.: 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

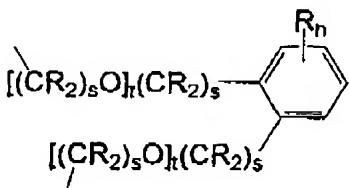
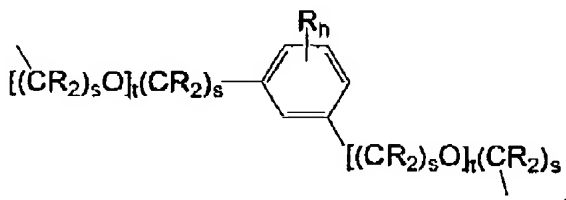
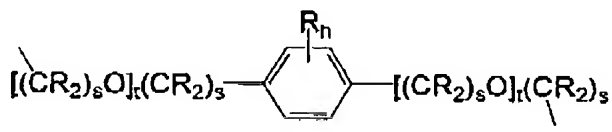
Docket No.: NBI-105CN

(CR'R'')₀₋₁₀(C₃-C₈ cycloalkyl), (CR'R'')₀₋₁₀CO₂R', or (CR'R'')₀₋₁₀OR' group, or the side chain of any naturally occurring amino acid; and

R' and R'' are each independently hydrogen, a C₁-C₅ alkyl, C₂-C₅ alkenyl, C₂-C₅ alkynyl, or aryl group, or R' and R'' taken together are a benzylidene group or a -(CH₂)₂O(CH₂)₂- group; and

1 ≤ f ≤ 8, 1 ≤ g ≤ 8, 0 ≤ h ≤ 4.

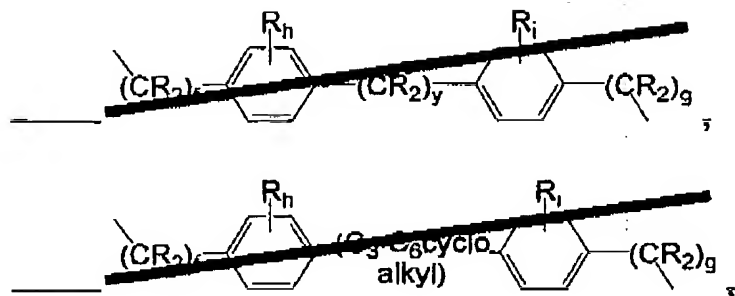
26. (original) The method according to claim 6, wherein said M group is a substituted or unsubstituted C₂-C₈ alkylene group, a substituted or unsubstituted C₁-C₈ alkenylene group, a substituted or unsubstituted C₂-C₈ alkynylene group.
27. (currently amended) The method according to claim 6, wherein said M group is



wherein 1 ≤ f ≤ 6, 0 ≤ g ≤ 6, 0 ≤ h ≤ 4, and each R group is independently a hydrogen or is selected from the group Z as defined in claim 5; or

Application No.: 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

Docket No.: NBI-105CN



wherein $1 \leq x \leq 10$ (preferably $1 \leq x \leq 4$), $1 \leq y \leq 8$, $1 \leq g \leq 8$, $0 \leq h \leq 4$, and $0 \leq i \leq 4$, and

each R group is independently a hydrogen or is selected from the group Z as defined in claim 5-a substituted or unsubstituted moiety selected from straight or branched alkyl, cycloalkyl, alkoxy, thioalkyl, alkenyl, alkynyl, heterocyclic, carbocyclic, aryl, aryloxy, aralkyl, aryloxyalkyl, arylacetamidoyl, alkylaryl, heteroaralkyl, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, or heteroaryl group, $(CR'R'')_{0-10}NR'R''$, $(CR'R'')_{0-10}CN$, NO_2 , halogen, $(CR'R'')_{0-10}C(halogen)_3$, $(CR'R'')_{0-10}CH(halogen)_2$, $(CR'R'')_{0-10}CH_2(halogen)_2$, $(CR'R'')_{0-10}CONR'R''$, $(CR'R'')_{0-10}(CNH)NR'R''$, $(CR'R'')_{0-10}S(O)_{1-2}NR'R''$, $(CR'R'')_{0-10}CHO$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(O)_{0-3}R'$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(CR'R'')_{0-3}H$, $(CR'R'')_{0-10}OH$, $(CR'R'')_{0-10}COR'$, $(CR'R'')_{0-10}(\text{substituted or unsubstituted phenyl})$, $(CR'R'')_{0-10}(C_3-C_8 \text{ cycloalkyl})$, $(CR'R'')_{0-10}CO_2R'$, or $(CR'R'')_{0-10}OR'$ group, or the side chain of any naturally occurring amino acid; and

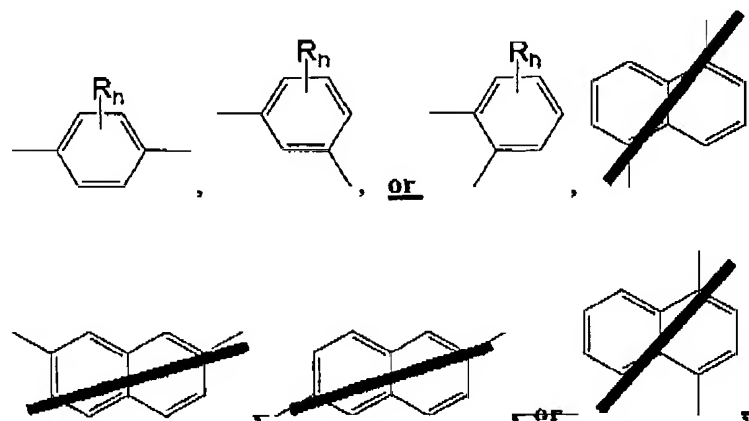
R' and R'' are each independently hydrogen, a C₁-C₅ alkyl, C₂-C₅ alkenyl, C₂-C₅ alkynyl, or aryl group, or R' and R'' taken together are a benzylidene group or a $-(CH_2)_2O(CH_2)_2-$ group.

- 28. (cancelled).
- 29. (cancelled).
- 30. (cancelled).

Application No.: 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

Docket No.: NBI-105CN

31. (currently amended) The method according to claim 6, wherein said M group is



wherein each R group is independently a hydrogen or is ~~selected from the group Z defined in claim 5~~, a substituted or unsubstituted moiety selected from straight or branched alkyl, cycloalkyl, alkoxy, thioalkyl, alkenyl, alkynyl, heterocyclic, carbocyclic, aryl, aryloxy, aralkyl, aryloxyalkyl, arylacetamidoyl, alkylaryl, heteroaralkyl, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, or heteroaryl group, $(CR'R'')_{0-10}NR'R''$, $(CR'R'')_{0-10}CN$, NO_2 , halogen, $(CR'R'')_{0-10}C(halogen)_3$, $(CR'R'')_{0-10}CH(halogen)_2$, $(CR'R'')_{0-10}CH_2(halogen)$, $(CR'R'')_{0-10}CONR'R''$, $(CR'R'')_{0-10}(CNH)NR'R''$, $(CR'R'')_{0-10}S(O)_{1-2}NR'R''$, $(CR'R'')_{0-10}CHO$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(O)_{0-3}R'$, $(CR'R'')_{0-10}O(CR'R'')_{0-10}H$, $(CR'R'')_{0-10}S(CR'R'')_{0-3}H$, $(CR'R'')_{0-10}OH$, $(CR'R'')_{0-10}COR'$, $(CR'R'')_{0-10}$ (substituted or unsubstituted phenyl), $(CR'R'')_{0-10}(C_3-C_8 \text{ cycloalkyl})$, $(CR'R'')_{0-10}CO_2R'$, or $(CR'R'')_{0-10}OR'$ group, or the side chain of any naturally occurring amino acid; and

R' and R'' are each independently hydrogen, a C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, or aryl group, or R' and R'' taken together are a benzylidene group or a $-(CH_2)_2O(CH_2)_2-$ group; and

$0 \leq h \leq 4$.

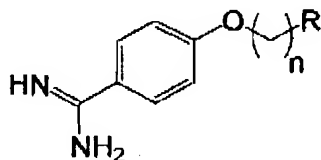
32. (cancelled).

33. (cancelled).

Application No.: 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

Docket No.: NBI-105CN

34. (cancelled).
35. (cancelled).
36. (cancelled).
37. (original) The method according to claim 2, wherein $m=1$, $n=0, 1$, or 2 , $p=0, 1$, or 2 , and $q=1$.
38. (original) The method according to claims 5, wherein $R^{a1}=R^{a2}$, $R^{b1}=R^{b2}$, $R^{c1}=R^{c2}$, $m=q$, $n=p$, and $Y^1=Y^2$.
39. (original) The method according to claim 6, wherein $R^1=R^2$, and $X^1=X^2$.
40. (original) The method according to claim 5, wherein said pharmaceutically acceptable salt is a hydrohalide salt or a 2-hydroxyethanesulfonate salt.
41. (cancelled).
42. (currently amended) A pharmaceutical composition for ~~the treatment of~~ for treating or preventing an amyloid-related disease comprising a compound according to claim 5.
43. (currently amended) The method according to claim 5, wherein said linking moiety is $-(CH_2)_n-$ (wherein n is 1, 2, or 3), $-NR^3-$ ~~wherein R^3 is as defined in claim 9~~, $-NH-$, $-S-$, $-O-$, $-NH-CH_2-$, or $-CH=CH-$, or combinations thereof; wherein R^3 is selected from the group consisting of hydrogen, substituted or unsubstituted straight or branched alkyl, cycloalkyl, carbocyclic, aryl, heterocyclic, and heteroaryl.
44. (currently amended) A chemical compound according to the formula:



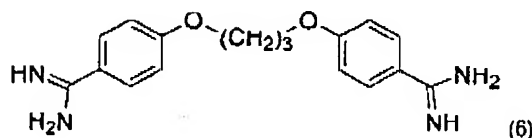
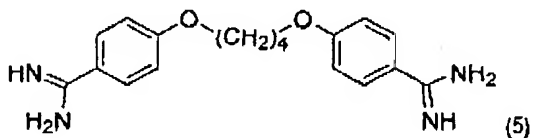
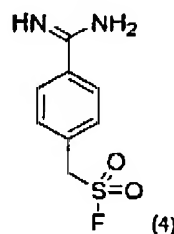
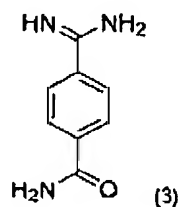
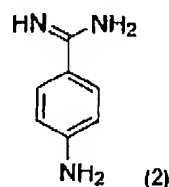
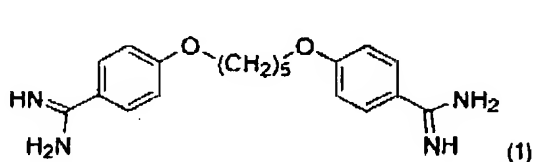
wherein n is an ~~interger~~ integer from 7 to 10, and R is Br or CO_2H , and pharmaceutically acceptable salts thereof.

45. (cancelled).

Application No.. 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

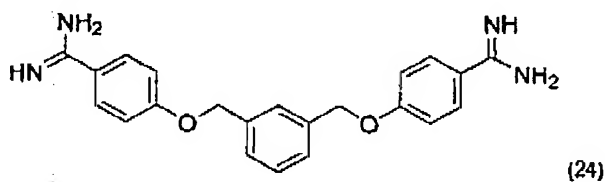
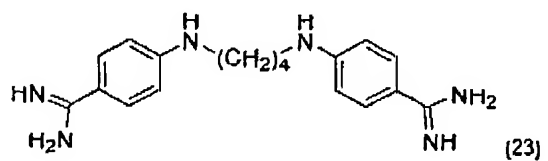
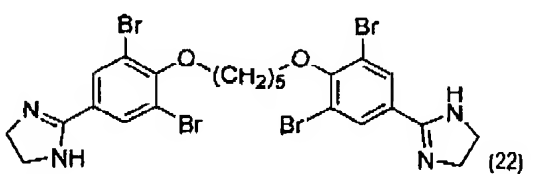
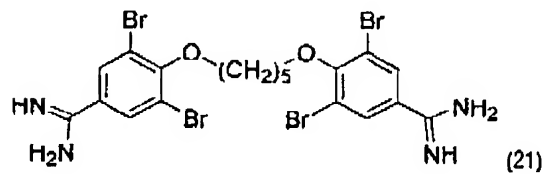
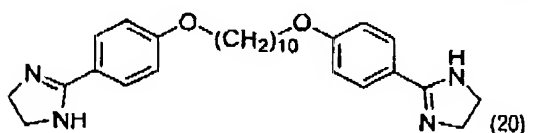
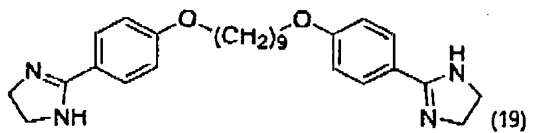
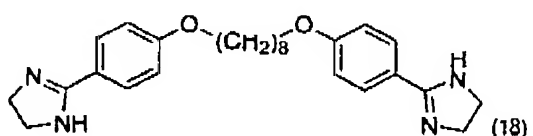
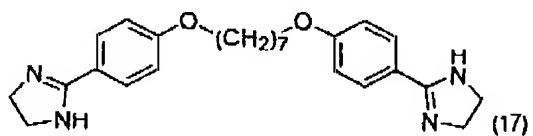
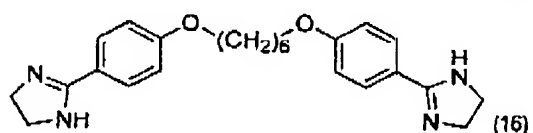
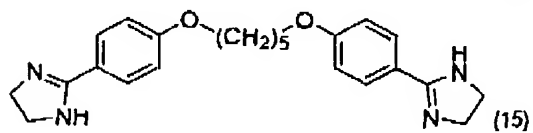
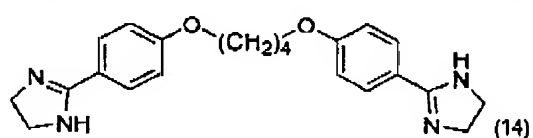
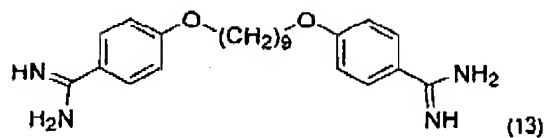
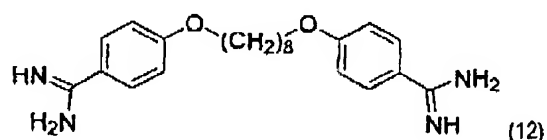
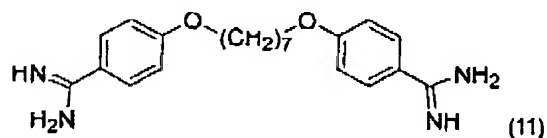
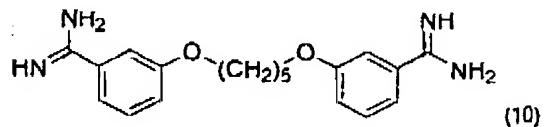
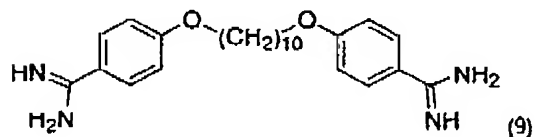
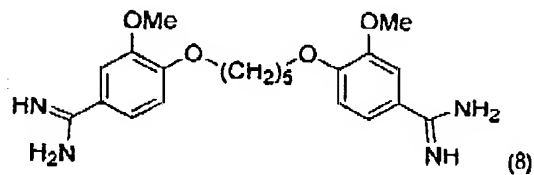
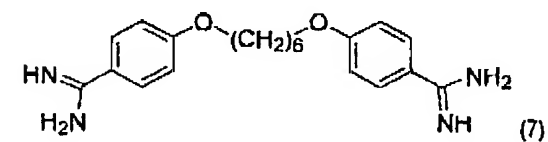
Docket No.. NBI-105CN

46. **(currently amended)** A pharmaceutical composition for treating or preventing an amyloid-related disease comprising a therapeutically effective amount of a chemical compound according to claim 44.
47. **(original)** The method of claim 1, wherein said amidine compound causes in an Alzheimer's patient a stabilization of cognitive function, prevention of a further decrease in cognitive function, or prevention, slowing, or stopping of disease progression.
48. **(currently amended)** The method according to claim 5, wherein Z is a substituted or unsubstituted moiety selected from straight or branched C₁-C₅ alkyl, C₃-C₈ cycloalkyl, C₁-C₆ alkoxy, C₁-C₆ thioalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, heterocyclic, carbocyclic, phenyl, phenoxy, benzyl, phenyloxyalkyl, arylacetamidoyl, alkylaryl, heteroaralkyl, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, or heteroaryl group, -NH₂, -CN, NO₂, F, Cl, Br, I, -CF₃, (CR'R'')₀₋₃CONR'R'', (CR'R'')₀₋₃(CNH)NR'R'', (CR'R'')₀₋₃S(O)₁₋₂NR'R'', (CR'R'')₀₋₃CHO, (CR'R'')₀₋₃O(CR'R'')₀₋₃H, -SO₃H, -CH₂OCH₃, -OCH₃, -SH, -SCH₃, -OH, (CR'R'')₀₋₃COR', (CR'R'')₀₋₃(substituted or unsubstituted phenyl), (CR'R'')₀₋₃(C₃-C₈ cycloalkyl), -CO₂H, or (CR'R'')₀₋₃OR' group.
49. **(new)** The method according to claim 1, wherein said compound is selected from the group consisting of



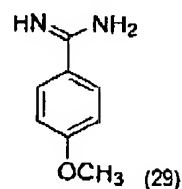
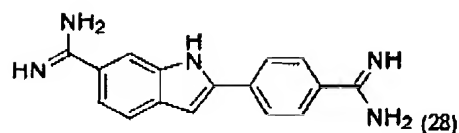
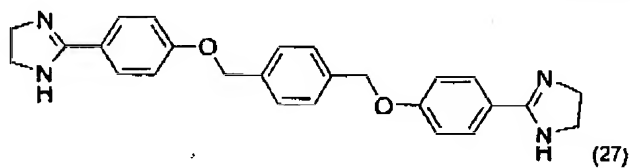
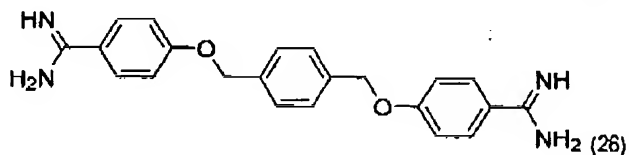
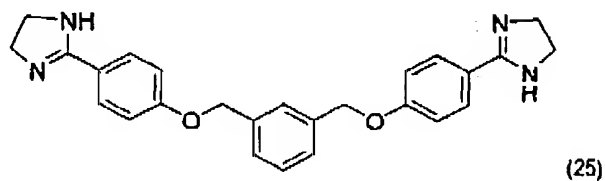
Application No.: 10/731,463
Preliminary Amendment
Filed February 09, 2004

Docket No.: NBI-105CN



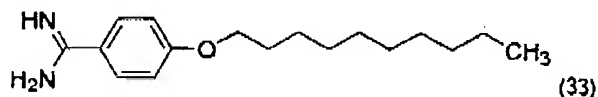
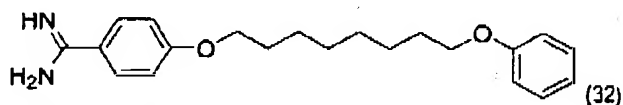
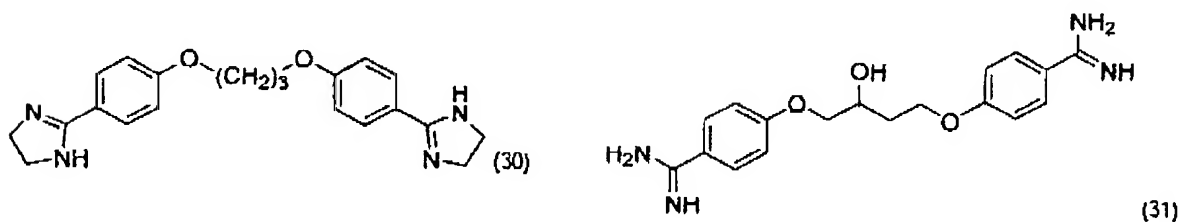
Application No.: 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

Docket No.: NBI-105CN



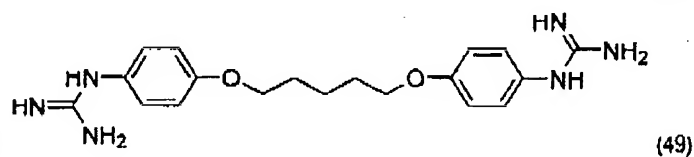
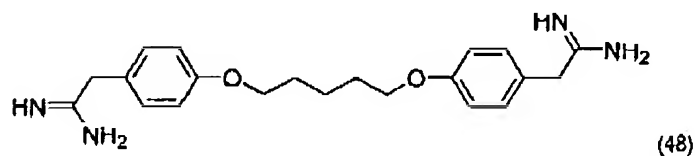
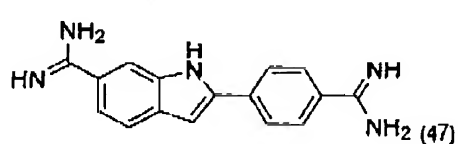
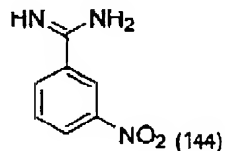
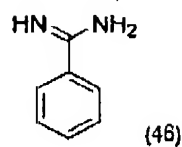
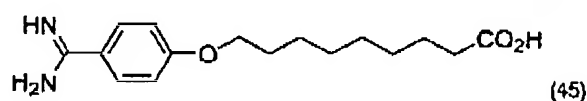
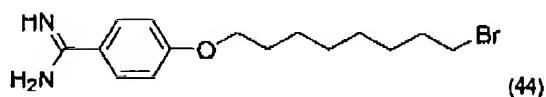
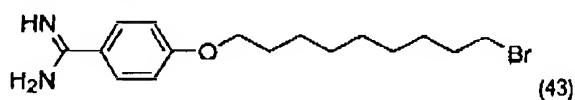
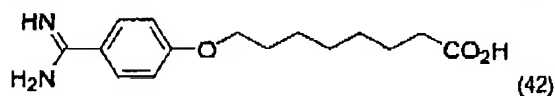
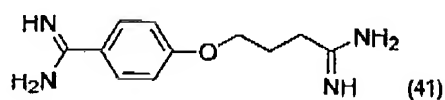
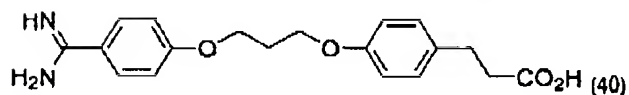
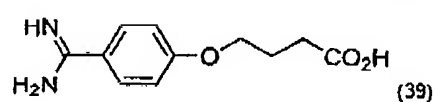
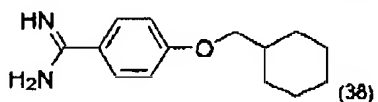
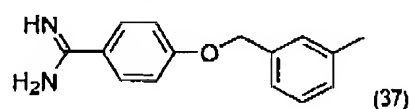
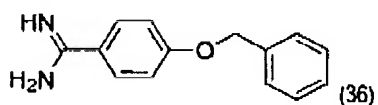
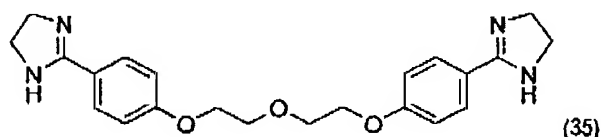
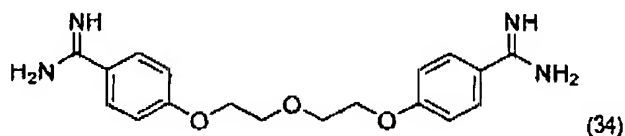
and pharmaceutically acceptable salts thereof.

50. (new) The method according to claim 1, wherein said compound is selected from the group consisting of



Application No.: 10/731,463
Preliminary Amendment
Filed February 09, 2004

Docket No : NBI-105CN

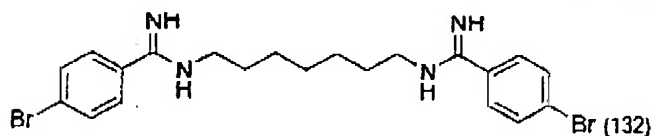
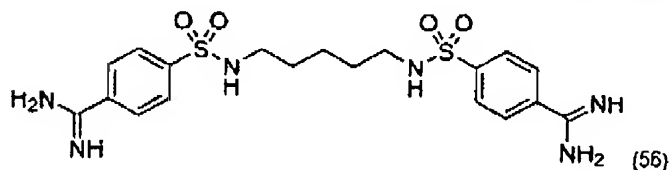
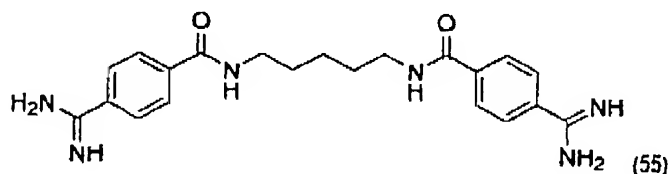
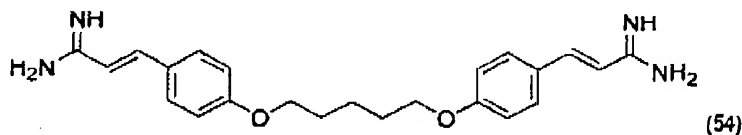
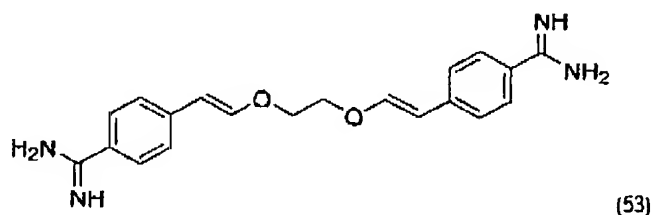
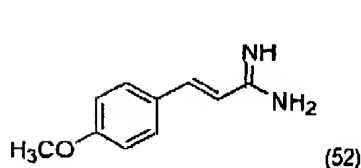
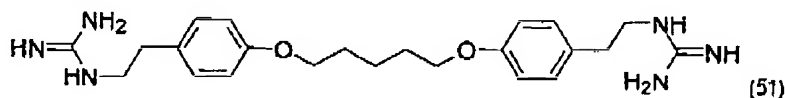
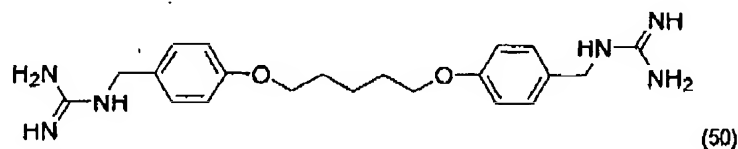


Application No.: 10/731,463
Preliminary Amendment
Filed February 09, 2004

Docket No.: NBI-105CN

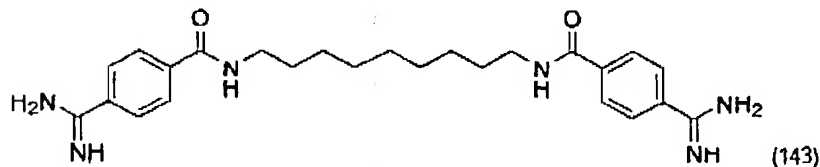
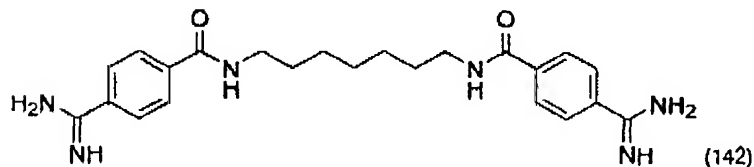
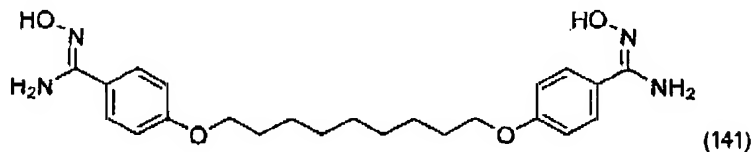
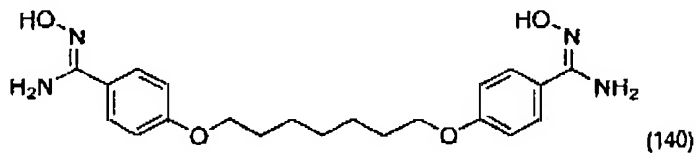
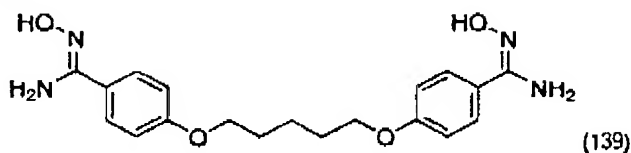
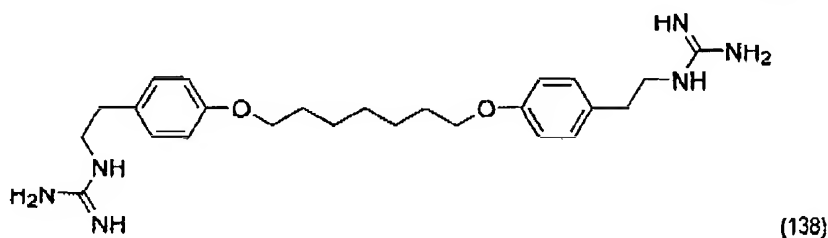
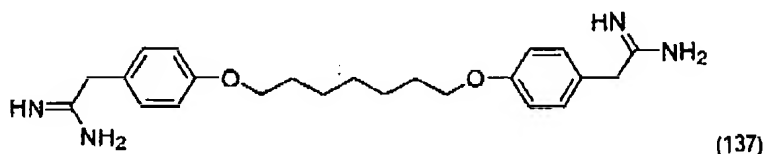
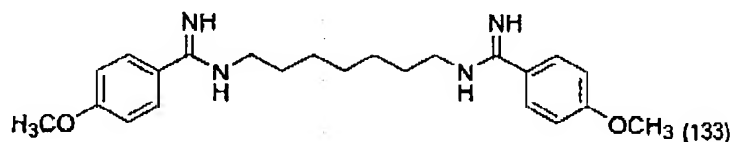
and pharmaceutically acceptable salts thereof.

51. (new) The method according to claim 1, wherein said compound is selected from the group consisting of



Application N. : 10/731,463
Preliminary Amendment
Filed February 09, 2004

Docket No.: NBI-105CN

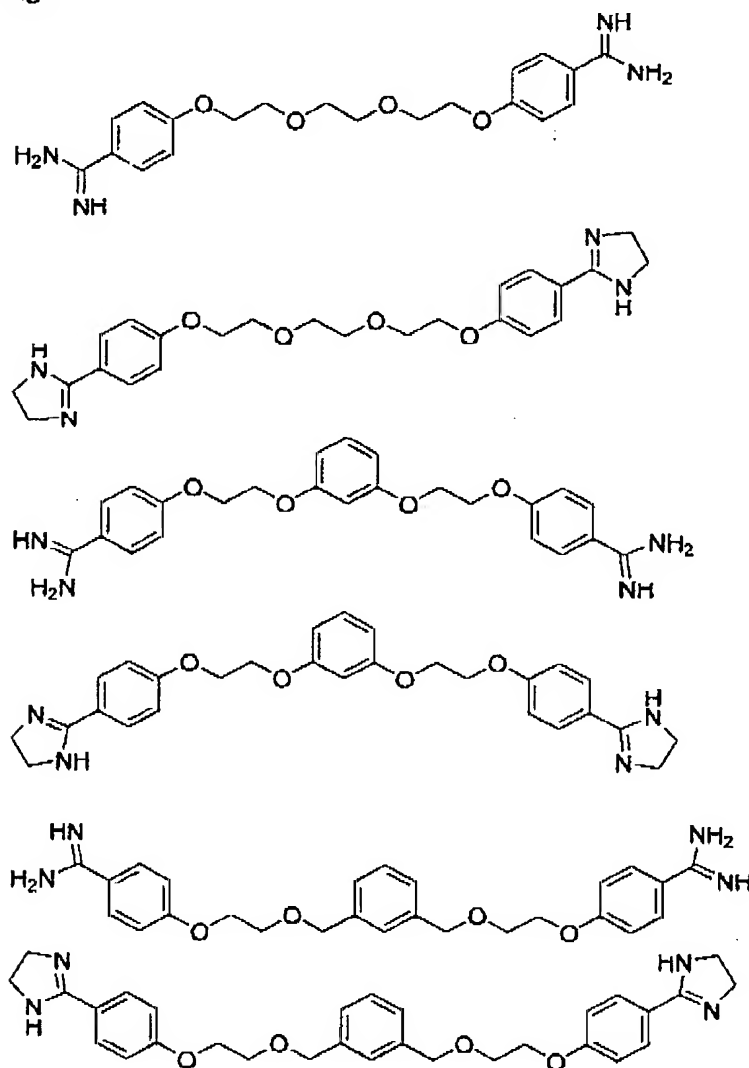


and pharmaceutically acceptable salts thereof.

Application No.: 10/731,463
Preliminary Amendment
Filed February 09, 2004

Docket No.: NBI-105CN

52. (new) The method according to claim 1, wherein said compound is selected from the group consisting of

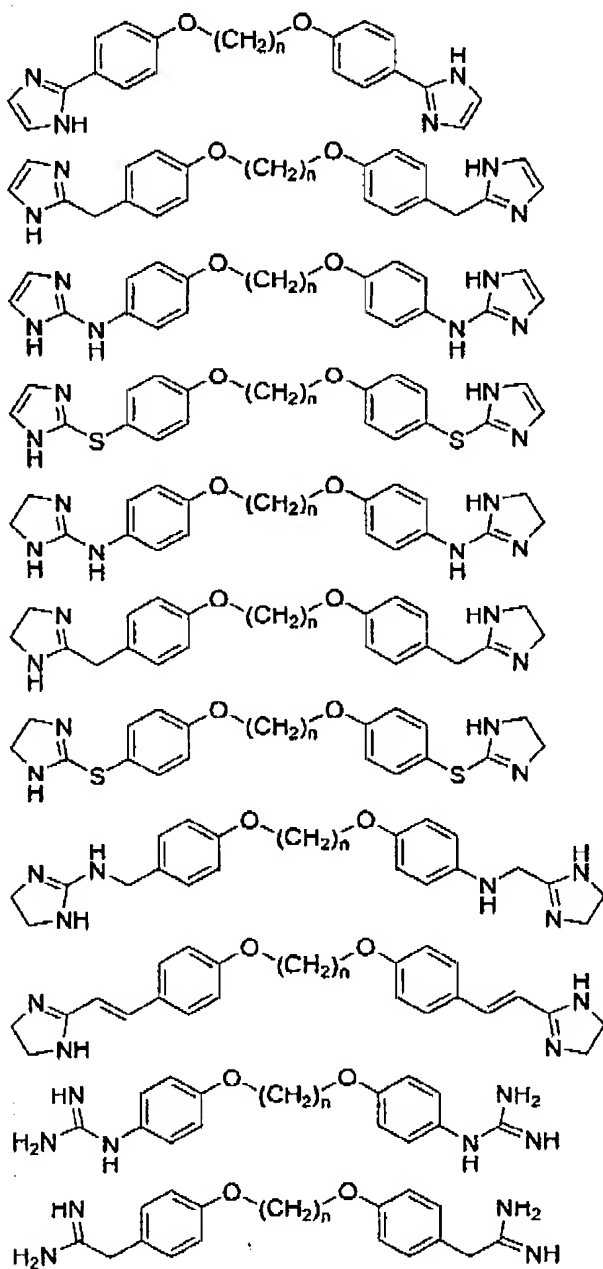


and pharmaceutically acceptable salts thereof.

Application No.: 10/731,463
Preliminary Amendment
Filed February 09, 2004

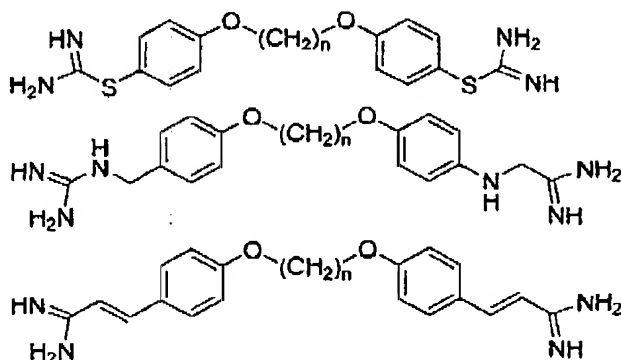
Docket No.: NBI-105CN

53. (new) The method according to claim 1, wherein said compound is selected from the group consisting of



Application No. 10/731,463
 Preliminary Amendment
 Filed February 09, 2004

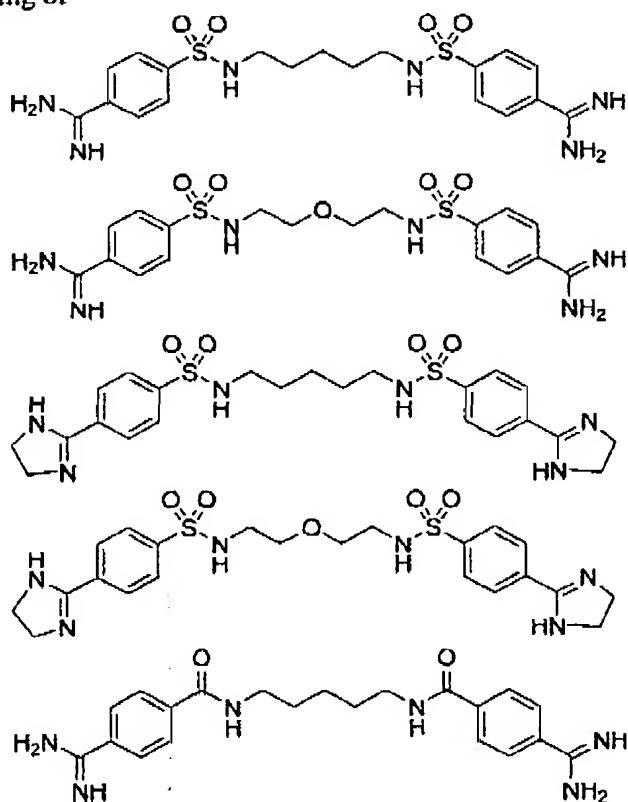
Docket No.: NBI-105CN



wherein n is an integer from 1 to 12,

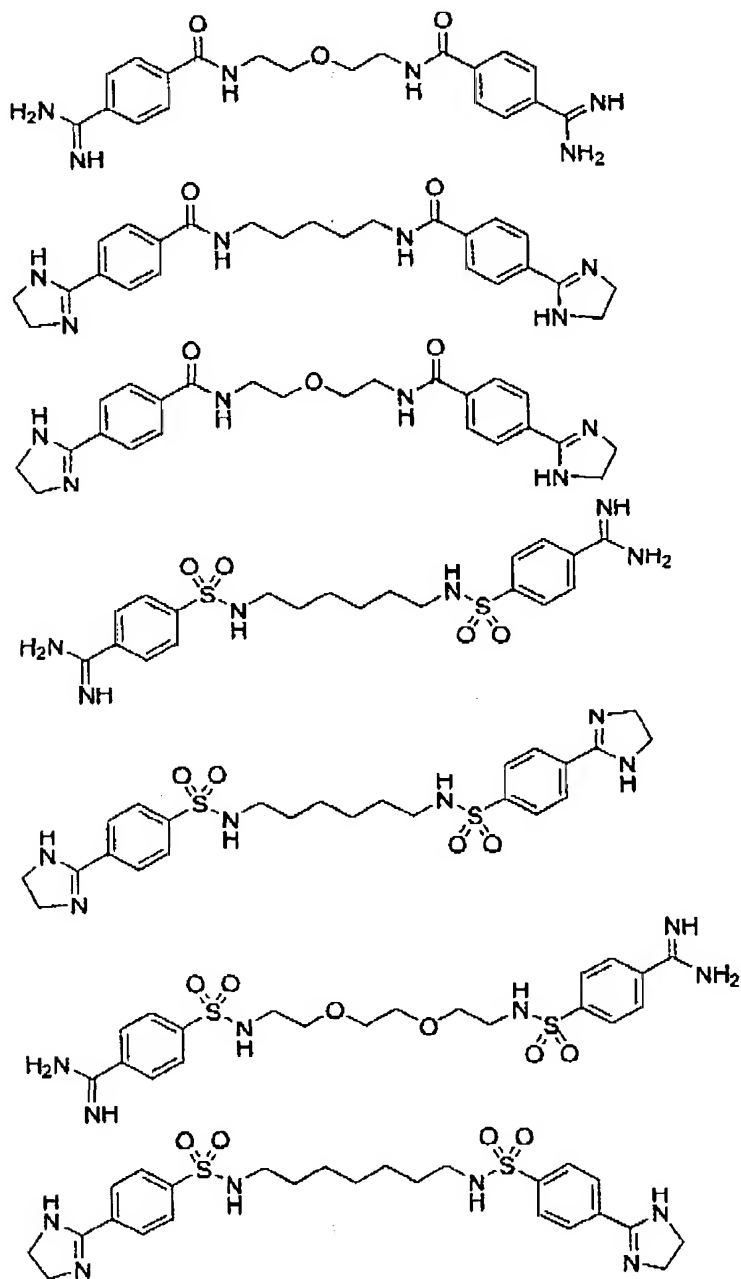
and pharmaceutically acceptable salts thereof.

54. (new) The method according to claim 1, wherein said compound is selected from the group consisting of



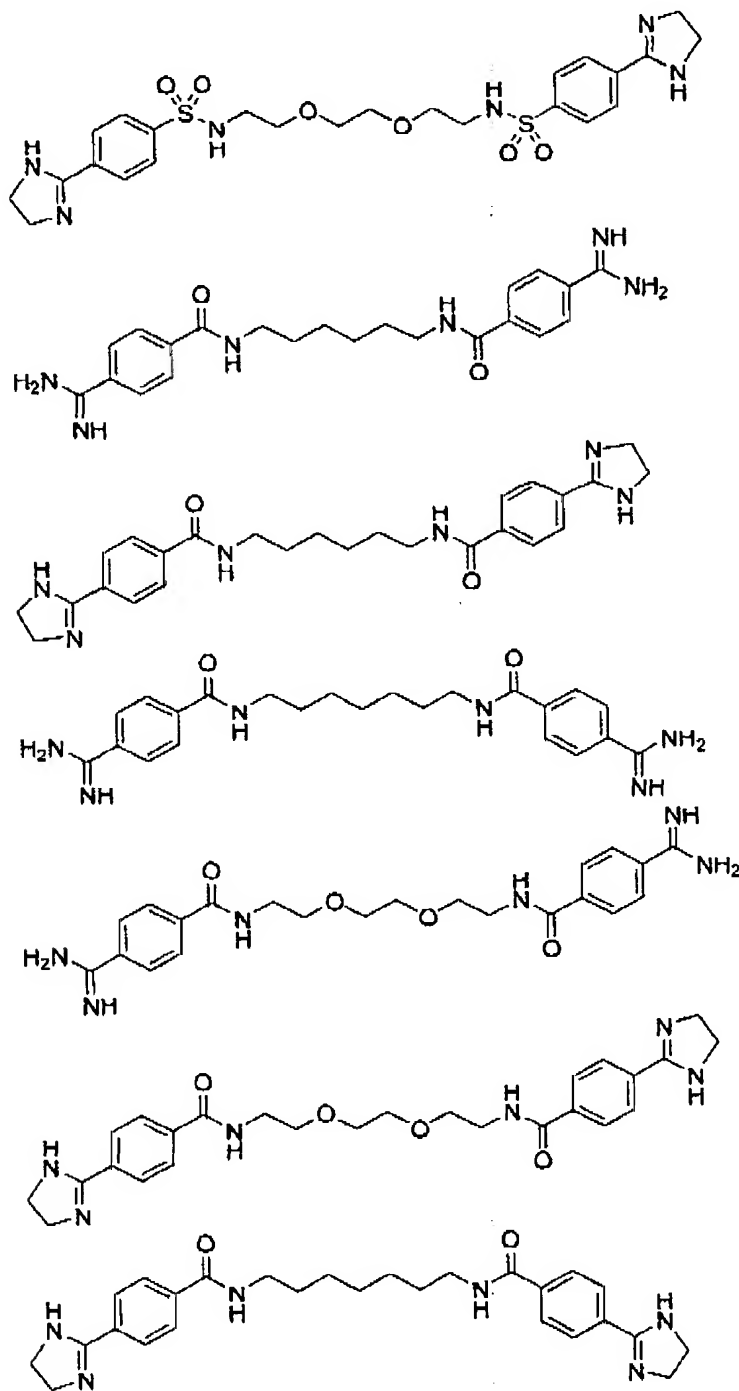
Application No.: 10/731,463
Preliminary Amendment
Filed February 09, 2004

Docket No.: NBI-105CN



Docket No.: NBI-105CN

Application No. 10/731,463
Preliminary Amendment
Filed February 09, 2004

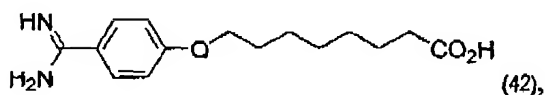


and pharmaceutically acceptable salts thereof.

Application No. 10/731,463
Preliminary Amendment
Filed February 09, 2004

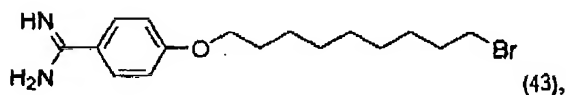
Docket No. NBI-105CN

55. (new) The method according to claim 1, wherein said compound is used therapeutically or prophylactically to treat a human in need thereof.
56. (new) The method according to claim 5, wherein said compound reduces or inhibits amyloid fibril formation or deposition, neurodegeneration, or cellular toxicity.
57. (new) A chemical compound having the following structure:



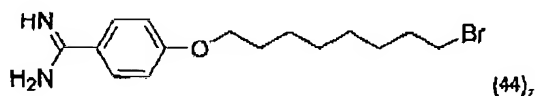
and pharmaceutically acceptable salts thereof.

58. (new) A chemical compound having the following structure:



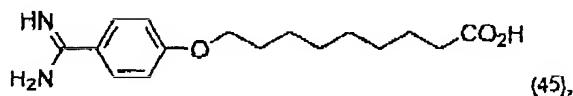
and pharmaceutically acceptable salts thereof.

59. (new) A chemical compound having the following structure:



and pharmaceutically acceptable salts thereof.

60. (new) A chemical compound having the following structure:



and pharmaceutically acceptable salts thereof.

61. (new) A pharmaceutical composition for treating or preventing an amyloid-related disease comprising a therapeutically effective amount of a chemical compound according to claim 44.